From: MS Outlook::Anastassios D. Retzios, Ph.D.
To:
Petrone, Michael at Roberts Pharmaceutical Corporation
cc:
MS Outlook::David Haenick (E-mail)
Subject: Serious Adverse Experience Definitions and Reporting
Date: 2:18 PM

Dear Michael:

In my comments regarding SAE reporting, I had asked GloboMax to update their definition of an SAE according to the updated CFRs. In their response, they indicated that they do not wish to do so, because their definition is included in the current CFRs. This is not accurate. The FDA did revise this definition in April 1, '99; I include the appropriate CFR sections as attachments. For brevity, I entered the new definitions for SAE and unexpected AEs below:

[Code of Federal Regulations]
[Title 21, Volume 5, Parts 300 to 499]
[Revised as of April 1, 1999]
From the U.S. Government Printing Office via GPO Access
[CITE: 21CFR312.32]
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Serious adverse drug experience: Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Unexpected adverse drug experience: Any adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. ``Unexpected,'' as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

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I am attaching copies of the two relevant CFR sections.

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